REMARKS

Reconsideration of the present application is respectfully requested in view of the amendments submitted herewith and the following remarks. Claims 1-2 and 18-23 were pending. Applicants note that under Disposition of Claims in the Office Action Summary and in the third paragraph of the Detailed Action, claim 17 is incorrectly listed as currently pending, which Applicants assume is an inadvertent typographical error. Applicants have hereby amended claims 1 and 19 and cancelled claims 22 and 23 without acquiescence to any rejection and without prejudice to filing a related divisional, continuation, or continuation-in part application. Accordingly, claims 1-2 and 18-21 are currently under examination. No new matter has been added to the application. Support for the amended claims may be found throughout the application, for example, at page 19, line 30 through page 20, line 4; at page 35, lines 9-25; and page 54, lines 6-19.

REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH (ENABLEMENT)

Claims 1, 2, 18, 19, 21, 22, and 23 stand rejected under 35 U.S.C. § 112, first paragraph, allegedly for lack of enablement. The Action concedes that the specification enables a method for identifying a leukemia of T cell, B cell, or myeloid lineage, wherein the sample is tissue fluid, blood, cerebrospinal fluid, lymphatic fluid, seminal fluid, bone marrow aspirate, and mucus and wherein the subject is human; however, the Action asserts that the specification does not enable a method wherein the biological sample is "generic cells," cell debris, cell extracts, serum, plasma, urine, and "generic aspirate," or wherein the subject is a non-human animal.

Applicants respectfully traverse these rejections and submit that the specification enables a person skilled in the art to make and use, without undue experimentation, the presently claimed methods. In view of the amendments submitted herewith, in which claims 1 and 19 have been amended and claims 22 and 23 have been cancelled without acquiescence to the rejection and without prejudice to further prosecution of any removed subject matter in a related divisional, continuation, or continuation-in-part application, Applicants submit that the basis for the rejections has been obviated.

The present claims are directed, in pertinent part, to a method for identifying a leukemia of T cell, B cell, or myeloid lineage in a human subject comprising contacting a

biological sample with an array of immunoglobulin molecules, wherein the biological sample, in certain embodiments, is tissue fluid, blood, cerebrospinal fluid, lymphatic fluid, seminal fluid, bone marrow aspirate, or mucus. The specification provides explicit and detailed guidance throughout the specification, including in working examples, enabling a skilled person to make and use the claimed methods, readily and without undue experimentation, for identifying a leukemia using any one of the biological samples that comprises cells from a human subject (*see, e.g.,* page 35, lines 20-25; page 37, line 25 through page 39, line 12; page 54, lines 6-19; and at page 61, lines 5-29; page 62, line 3 through page 65, line 30).

Applicants therefore respectfully submit that the Application satisfies the requirements for enablement under 35 U.S.C. § 112, first paragraph, and request that the rejection of the claims be withdrawn.

REJECTIONS UNDER 35 U.S.C. § 103

Claims 1, 2, 19, 20, and 22 stand rejected under 35 U.S.C. § 103, allegedly for being obvious over Sundberg et al. (*J. Am. Chem. Soc.* 117:12050-57 (1995)) in view of the Becton Dickinson Acute Leukemia Phenotyping Kit (Becton Dickinson). The Action concedes that Sundberg et al. fail to teach or suggest a method for diagnosing leukemia or for detecting leukemic cells by using "a patterned array of antibodies." The Action, however, asserts that Sundberg et al. teach a "general method of immobilizing antibodies at precise locations on solid supports" and that "the technique is amenable for creating a patterned array with a high degree of spatial orientation." The Action concedes the Becton Dickinson document fails to teach the use of a patterned antibody array that comprises the monoclonal antibodies as recited in the claims; however, the Action alleges that Becton Dickinson teaches using twelve monoclonal antibodies that provide a pattern of antibody binding indicative of leukemia. The Action asserts that the presently claimed embodiment of Applicants' invention would have been *prima facie* obvious at the time of filing the instant application to use the antibodies taught by Becton Dickinson in an array described by Sundberg et al.

Applicants respectfully traverse this ground of rejection and submit that the instant claims meet the requirements for nonobviousness. To establish a *prima facie* case of obviousness the Action must show (1) that the references teach or suggest all claim limitations;

(2) that the references provide some teaching, suggestion, or motivation to combine or modify the teachings of the prior art to produce the claimed invention; and (3) that the combined teachings of the references indicate that by combining the references, a person having ordinary skill in the art will achieve the claimed invention with a reasonable expectation of success. When rejection of claims depends upon a combination of prior art references, something in the prior art as a whole must suggest the desirability, thus the obviousness, of making the combination (*see In re Rouffet*, 149 F.3d 1350, 1355, 47 U.S.P.Q.2d 1453 (Fed. Cir. 1998)).

The present claims are directed to a method for identifying a leukemia of T cell, B cell, or myeloid lineage in a human subject, comprising contacting a biological sample comprising leukocytes from the human subject with an array of immunoglobulin molecules immobilized to a solid support. The array comprises 7 to about 1000 immunoglobulins, wherein the immunoglobulin molecules are specific for cell surface marker antigens, and wherein the cell surface marker antigens comprise at least seven cell surface marker antigens selected from the list in Table 4. The cell surface marker antigens distinguish leukemias of T cell, B cell, or myeloid lineage, and by determining which cell surface marker antigens have bound to which immobilized immunoglobulin molecules, a differential pattern of density of binding is established that identifies a leukemia that is of T cell, B cell, or myeloid lineage.

The cited documents, either alone or in combination, fail to teach each feature of the present claims. Neither Sundberg et al. nor Becton Dickinson teach a method for identifying a leukemia of T cell, B cell, or myeloid lineage that comprises permitting binding a biological sample that comprises cells from a human subject with an array of 7 to about 1000 immunoglobulins. The cited documents, alone or in combination, also fail to describe that a method for determining whether a leukemia is of T cell, B cell, or myeloid lineage comprises establishing a differential pattern of density of binding of the cells in the biological sample with the array of immunoglobulins. As conceded by the Action, Sundberg et al. fail to describe a method for detecting leukemia or any cancer. Sundberg et al. instead merely teach a complicated method for attaching macromolecules to a support. When Sundberg et al. teach binding of antibodies to a support, Sundberg et al. describe binding *of only two* different antibodies to a flow cell. Furthermore, Sundberg et al. teach that a limitation of their method "is its reliance on serial rounds of photodeprotection and immobilization, which may *restrict* its application to the

creation of *fairly simple arrays* of biomolecules (*see* Sundberg et al., at page 12056, second column, lines 11-14) (emphasis added). Thus, Sundberg et al. teach a way from the claimed method that comprises contacting a biological sample with an array of 7 to about 1000 immunoglobulin molecules that are immobilized to a solid support. Moreover, Sundberg et al. are silent regarding establishing a differential pattern of density of binding of the immobilized immunoglobulin molecules with cell surface marker antigens that are expressed on the cell surface of cells in the biological sample. Accordingly, a person having ordinary skill in the art would have no reasonable expectation of successfully achieving the claimed methods.

The teachings of Becton Dickinson fail to remedy the deficiencies of Sundberg et al. Becton Dickinson fail to teach or suggest a method for identifying a leukemia by contacting a biological sample with an array of 7 to about 1000 immunoglobulins that are immobilized on a solid support. Also, as conceded by the Action, Becton Dickinson further fail to teach or suggest that a differential pattern of density of binding is obtained when cell surface marker antigens expressed on cells in a biological sample are contacted with the array of immunoglobulin molecules. Becton Dickinson instead describe an entirely different method, flow cytometry.

Neither cited document provides any requisite teaching, suggestion, or motivation to combine the teachings of either document or to modify the methods taught in either document to obtain Applicants' claimed methods. Even assuming *arguendo,* as the Action asserts, that a person having ordinary skill in the art would be motivated to detect a leukemia of T cell, B cell, or myeloid lineage using the antibodies described by Becton Dickinson and eliminate the expense of flow cytometry, an ordinarily skilled artisan would not be motivated to modify the teachings of Sundberg et al. to obtain the claimed methods. As discussed above, Sundberg et al. teach that their method may be limited to simple arrays of biomolecules. Sundberg et al. further teach that immobilization methods other than those described therein may not permit immobilization of different biomolecules to the same surface (*see* Introduction). Thus, Sundberg et al. suggest that any modification to the method described therein would render the method inoperable for its intended purpose.

Therefore, the cited documents, alone or in combination, fail to teach or suggest each and every feature of the presently claimed methods, and neither document alone or in combination provides any teaching, motivation, or suggestion of the desirability to modify either

method to obtain Applicants' claimed embodiments. Applicants submit that the Action has failed to establish a *prima facie* case of obviousness and request that this rejection be withdrawn.

Claims 1, 2, 18, 19, 20, and 22 stand rejected under 35 U.S.C. § 103, allegedly for being obvious over Sundberg et al. in view of Becton Dickinson and further in view of Paul (*Fundamental Immunology* (1993) page 460). The Action asserts that Paul teaches the advantages of using polyclonal antibodies instead of monoclonal antibodies for diagnostic methods and that a person having ordinary skill in the art would have found obtaining Applicants' claimed method obvious by combining the teachings of Sundberg et al., Becton Dickinson, and Paul.

Applicants respectfully traverse this rejection and submit that the claimed methods are nonobvious as required under 35 U.S.C. § 103. Applicants refer the Examiner to the discussion above that Sundberg et al. in view of Becton Dickinson fail to teach or suggest each feature of the claimed method for identifying a leukemia of T cell, B cell, or myeloid lineage and further fail to provide any motivation, teaching, or suggestion to combine or modify the teachings of either or both documents to obtain successfully the presently claimed embodiments of Applicants' invention. Paul fails to remedy the deficiencies of Sundberg et al. and Becton Dickinson.

Applicants respectfully disagree with the Action that Paul teach advantages of polyclonal antibodies over monoclonal antibodies in diagnostics and disagree that Paul provides any motivation, teaching, or suggestion to use either monoclonal antibodies or polyclonal antibodies preferentially in the claimed method. Applicants cannot find any description in the page from Paul provided by the Action that polyclonal antibodies are more useful than monoclonal antibodies for diagnostic purposes. Paul et al. teach that polyclonal sera may have an advantage for use in certain immunoassay techniques such as immunoprecipitation, which may benefit from the multivalency of polyclonal antisera. Immunoprecipitation is a different immunoassay method than that described by Sundberg et al., Becton Dickinson, and by the present application. Applicants submit that Paul provides nothing more than a cumulative reference that monoclonal antibodies and polyclonal antisera have different characteristics that a

person skilled in the art may wish to consider when contemplating use of an immunoglobulin source.

Applicants therefore submit that the present claims are nonobvious over Sundberg et al. in view of Becton Dickinson and in further view of Paul and respectfully request that this rejection be withdrawn.

Claims 1, 2, and 19-22 also stand rejected under under 35 U.S.C. § 103, allegedly for being obvious over Sundberg et al. and Becton Dickinson and in further view of Terstappen et al. (U.S. Patent No. 6,265,150). The Action asserts that Terstappen et al. teach a method of rapidly obtaining human antibodies against known and novel surface antigens and that a person having ordinary skill in the art would have been motivated to use a library of phage particles expressing antibody fragments as a renewable source of antibody fragments for use in the claimed method.

Applicants respectfully traverse this rejection and submit that the Action has failed to establish a *prima facie* case of obviousness and that the presently claimed method is nonobvious over Sundberg et al. and Becton Dickinson in further view of Terstappen et al. Applicants refer the Examiner to the discussion above that Sundberg et al. in view of Becton Dickinson fail to teach or suggest each feature of the claimed method for identifying a leukemia of T cell, B cell, or myeloid lineage and further fail to provide any motivation, teaching, or suggestion to combine or modify the teachings of either or both documents to obtain successfully the presently claimed embodiments of Applicants' invention. Terstappen et al. fail to remedy the deficiencies of Sundberg et al. and Becton Dickinson.

Terstappen et al. fail to teach or suggest a method for identifying a leukemia of T cell, B cell, or myeloid lineage comprising contacting a biological sample comprising leukocytes from a human subject with an array of immunoglobulin molecules immobilized to a solid support. Terstappen et al. fail to teach that the array comprises 7 to about 1000 immunoglobulins, wherein the immunoglobulin molecules are specific for cell surface marker antigens, and wherein the cell surface marker antigens comprise at least seven cell surface marker antigens selected from the list in Table 4 of the present application. Terstappen et al. also fail to teach or suggest that the cell surface marker antigens distinguish leukemias of T cell, B

cell, or myeloid lineage, and by determining which cell surface marker antigens have bound to which immobilized immunoglobulin molecules, a differential pattern of density of binding is established that identifies a leukemia that is of T cell, B cell, or myeloid lineage. Terstappen et al. merely teach one of several methods practiced in the art at the time the present application was filed for obtaining immunoglobulin fragments.

Applicants therefore submit that the Action has not established a *prima facie* case of obviousness of the presently claimed subject matter over Sundberg et al. in view of Becton Dickinson and in further view of Terstappen et al. Applicants further submit that the present claims satisfy the requirements for nonobviousness under 35 U.S.C. § 103, and request that all rejections of the claims be withdrawn.

Applicants respectfully submit that all claims in the application are allowable. Favorable consideration and a Notice of Allowance are earnestly solicited. In the event that the Examiner believes a teleconference will facilitate prosecution of this case, the Examiner is invited to telephone the undersigned at 206-622-4900.

Respectfully submitted,

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